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By CHARLES F. CRAIG,
Captain, Medical Corps, U. S. Army,
Washington, D. C.

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VOLUME III DECEMBER, 1910 NUMBER 11

THE SOUTHERN
MEDICAL JOURNAL

Journal of the Southern Medical Association

Incorporating the Gulf States Journal of Medicine and Surgery and Mobile Medical and Surgical Journal

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Price $2.00 Per Annum Single Number 20 Cents

Reprint From
The Southern Medical Journal.
February, 1912. Pages 50-57.

22200147497

REPRINT FROM
THE SOUTHERN MEDICAL JOURNAL
FEBRUARY, 1912, PAGES 50-57

IMPORTANT FACTORS IN THE PROPHYLAXIS OF THE MALARIAL FEVERS*

By CHARLES F. CRAIG,
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The discovery of the relation of the mosquito to the transmission of the malarial fevers placed the prophylaxis of these infections upon a scientific basis, and much has been accomplished by the destruction of these insects, or by protecting man from their bites. While this is true, it must be admitted that in many, if not most, localities in the tropics or subtropics, a complete eradication of mosquitoes is an impossibility, and other methods of prophylaxis have to be resorted to in order to achieve success in the prevention of malarial disease.

We now know that malaria is transmitted to man by certain species of mosquitoes, and that if it were possible to either destroy all malaria-carrying mosquitoes, or kill all the plasmodia in the blood of infected individuals, we would succeed in preventing malarial infection in any locality. While this is theoretically possible we know also in most instances it is practically impossible and hence we are forced to combine methods looking both to the destruction of the mosquito and the plasmodia.

In order that prophylactic measures be successful it is also essential that we have the support of the public, and therefore the education of the latter regarding the etiology and prophylaxis of malaria becomes of prime importance in any campaign against these infections.

In this paper I desire to call your attention to three factors which appear to me to be of great importance in malarial prophylaxis—*i. e., the discovery of latent infections; the proper treatment of initial and latent infections; and the education of the public.*

The Discovery of Latent Infections. By a latent malarial infection we understand one in which the plasmodia may be demonstrated in the blood, but in which no clinical symptoms of sufficient gravity to attract attention are observed. The term includes both those instances in which no definite symptoms of malaria have ever been present, and those cases in which the disease is latent in the intervals between recurrences. While in many latent infections no definite clinical symptoms are present, if one takes the temperature of the patient it will often be found above normal, and careful inquiry will elicit the fact that the patient suffers more or less from headache, loss of appetite, and general malaise.

It is well known that in malarial localities a considerable proportion of individuals in apparently good health are carriers of the plasmodia, and that the natives of such regions possess an acquired immunity to the usual effects of the malarial toxin. The history of such acquired immunity is that of repeated attacks of malarial fever, each one a little less severe than the one preceding, until at last a clinical cure is effected. However, most individuals who possess this acquired immunity show malarial plasmodia in the blood at intervals, so that the immunity really consists in a tolerance to the toxin or toxins, and any unusual strain or exposure will often result in an acute attack of the disease in such individuals.

*Read before the Southern Medical Association, at Hattiesburg, Miss., Nov. 14-17, 1911, and published with the permission of the Surgeon-General of the United States Army.

It is obvious that while these individuals are fortunate in possessing a tolerance to the malarial toxin, they are dangerous to those surrounding them, as they are carriers of the plasmodia, and are thus able to infect mosquitoes.

It has also been demonstrated that latent infections are especially prevalent among children, although in most malarial localities the plasmodia have also been found in a large percentage of the adult population. Koch[1], from his observations in Africa, concluded that latent infection was practically confined to children, and his observations were soon confirmed by Thomas[2], Stephens and Christophers[3] and by James[4], but many other authorities have since proven that latent infection is very frequent in adults, and that the true index of the prevalence of these fevers in any region can only be determined by the examination of the blood of both children and adults.

The following tables give the results of several investigators as regards the prevalence of latent malaria in children, in various localities:

TABLE I.

Koch's Observations in Kaiser Wilhelm's Land, New Guinea.

Place	Age	No. Examined	Percentage Infected
Bogadjine..	Under 2 years	10	8 cases or 80. %
Bogadjine..	2 to 5 years	12	5 cases or 41.6%
Bogadjine..	5 to 55 years	86	0 cases or 0. %
Bongn.....	Under 2 years	6	6 cases or 100. %
Bongn.....	2 to 5 years	13	6 cases or 46.1%
Bongn.....	5 to 10 years	17	4 cases or 23.5%
Bongn.....	10 to 40 years	39	0 cases or 0. %

TABLE II.

Thomas's Observations in Manos, North Brazil.

Age	No. Examined	Plasmodia Present	Percentage
6 mos. to 2 yrs...	9	3	33.3
2 yrs. to 5 yrs...	38	20	52.6
5 yrs. to 8 yrs...	51	28	54.9
8 yrs. to 10 yrs...	59	27	45.7
Totals	157	78	49.6

At Accra, West Africa, Stephens and Christopher found from 23 to 90 per cent of babies infected; up to 8 years of age, 20 to 57 per cent; up to 12 years of age, 28 to 30 per cent; and after the twelfth year infection was found to be rare.

James, in India, found the percentage of latent infection in native children to vary greatly in different localities. At Mian Mir, children up to 2 years of age showed 80 per cent infected; up to 5 years, 66 per cent; up to 10 years, 50 per cent; while children older than 10 years showed no infection. At Ennur, children up to 3 years of age showed 65 per cent infected; up to 5 years, 51 per cent; up to 10 years, 46 per cent; and up to 15 years, 16 per cent. He found no infection in natives over 15 years of age.

Annett, Dutton, and Elliott's[5] observations are given in the following table:

TABLE III.

Annett, Dutton, and Elliott's Observations in Nigeria, Africa.

Age of Child	Per Cent Infected
0 to 1 year	27.3%
1 to 2 years	63.0%
2 to 3 years	63.0%
3 to 4 years	51.0%
4 to 5 years	48.8%
5 to 6 years	34.8%
6 to 7 years	6.6%
7 to 8 years	27.5%
8 to 9 years	25.0%
9 to 10 years	14.0%
10 years and above	10.0%

At Camp Stotsensburg, one of the most malarial localities in the Philippine Islands, I[6] examined the blood of 45 native adults and 180 native children, all of whom at the time of examination were free from symptoms of malaria. The following table gives the result of these examinations, but only includes 147 of the children, as only in this number could I obtain the exact age:

TABLE IV.

Observations at Camp Stotsenburg, Island of Luzon, Philipppines.

Age	No. Examined	No. Infected	Per Cent Infected
1 to 5 yrs.....	40	30	72.5%
5 to 10 yrs.....	54	20	37.0%
10 to 15 yrs.....	53	13	24.5%
Adults	45	28	62.2%
Totals	192	91	47.4%

The large percentage of adults showing latent infection in this locality was contrary to the reports of Koch, Stephens and Christophers, and James, that only the children in malarial localities were thus affected to any extent, but my observations have since been confirmed, in different localities, by Ollwig[7], Panse[8], A. Plehn[9], Darling[10], the Sergents[11], Hope, and others. The following tables give the results of these observers:

TABLE V.

Ollwig's Observations in Dutch East Africa.

Age	No. Examined	Plasmodia Present	Percentage
Under 1 year	93	33	35.4
1 yr. to 5 yrs.....	220	83	37.7
5 yrs. to 15 yrs.....	971	109	11.2
Adults	650	105	16.1
Totals	1,934	330	17.0

TABLE VI.

Panse's Observations in Tonga, East Africa.

Age	No. Examined	No. Infected	Per Cent Infected
Under ½ yr.....	16	6	37.5%
Between ½ and 1 yr.	9	6	66.6%
1 year of age.....	25	22	88.0%
2 years of age	20	17	85.0%
3 years of age	28	25	89.2%
Between 4 and 5 yrs.	48	34	70.8%
Between 6 and 7 yrs.	84	52	61.9%
Half-grown children .	314	125	39.4%
Adults	1,683	258	15.3%

TABLE VII.

A. Plehn's Observations in The Kameruns, West Africa.

Age	No. Examined	No. Infected	Per Cent Infected
Under 2 years.....	18	17	94%
Between 2 and 5 yrs.	26	24	92%
Between 5 and 10 yrs.	40	34	85%
Adults	43	26	60%
Totals	127	101	79.5

In the Canal Zone, Darling found latent infections in 10 per cent of all laborers examined, while 30 per cent of West India laborers were found infected, despite the fact that these laborers had been exposed to malaria since infancy, thus showing that their immunity consisted in a tolerance to the toxin of the plasmodia rather than to the plasmodia.

TABLE VIII.

Sergents' Observations in Algeria, Africa.

Age	No. Examined	Plasmodia Present	Percentage
1 to 5 years	1,316	267	20.2
6 to 10 years	1,360	326	23.9
11 to 15 years..	933	272	29.1
Adults	2,471	722	33.2
Totals	6,080	1,587	26.1

of 3,609 children examined, 867, or 23.9 per cent, were infected.

Of 2,471 adults examined, 722, or 33.2 per cent, were infected.

In Pabna, Hope found that while 922 adult natives showed plasmodia in their blood, only 862 children examined at the same time presented them; in other words that the adult malarial ratio was higher than the ratio in children.

Consolidating the reports given above, regarding the prevalence of latent infection, at various ages, we reach the following results:

TABLE IX.

Prevalence of Latent Infection at Various Ages. Consolidated Table.

Age	No. Examined	No. Infected	Per Cent Infected
1 to 5 years	1,684	502	29.8
5 to 10 years ...	1,645	463	28.1
10 to 15 years...	1,390	437	31.4
Adults	4,931	1,139	23.0
Totals	9,650	2,541	26.3

A study of this table shows the percentage of latent infections varies but little in adults or children in badly infected localities, and that it is just as important to determine the percentage of infected adults as of children, if one desires to know the exact malarial index of any region.

From the summary of the observations given it is evident that latent infection must be considered a most important factor in malarial prophylaxis, as a large percentage of such individuals have developed *gametes*, the active agents in transmitting the disease to the mosquito. From my own observations I believe that about 50 per cent of latent cases are *gamete carriers*, and it is easy to calculate

the immense harm such cases do in regions where proper species of mosquitoes are present, when one remembers the large number of latent infections in such localities.

Admitting then the importance of the discovery of these cases of latent malaria, the question arises, what are the most practicable methods available for determining their number in any locality? In many regions it is possible to enforce a blood examination of the natives, and thus it is easy to discover the amount of latent infection. In our own country this can only be accomplished with the co-operation of the public, and by competent physicians detailed by State or local boards of health. In every malarial locality an effort should be made to educate the people regarding the importance of latent infections, and after they have once realized this they will gladly submit to a blood examination. In such localities all school children should be examined, and, if possible, the adult population, and those found infected should be properly treated until a blood examination results negatively.

We have accomplished but little in this country in this respect, the observations of Sims and Warwick, at Taladega, Ala., being the only ones I know of in which an effort has been made to determine the amount of latent infection in children. These observers found that between 8 and 9 per cent of the children examined by them showed latent infection, and that of these only 3 1-2 per cent developed symptoms in five months. Such observations are of the greatest practical value, and should be repeated in every malarial locality. After a preliminary educational campaign it should be possible for the State or local boards of health to undertake the examination of the blood of both adults and children in badly infected districts, and it is obvious that the proper treatment of all cases of latent infection thus discovered would do much in lowering the malarial rate in these localities. The examination of the children relative to enlargement of the spleen would be a useful method in our own country, but, in my opinion, is far inferior to the examination of the blood. The discovery of latent infection depends upon an examination of the blood of both children and adults, and if physicians in malarial regions would insist upon such examination in all cases coming to them, a large number of infections would be discovered and properly treated.

Municipal and State boards of health should provide for the free examination of blood so that physicians who are unable to make examinations can have them made easily and promptly, and the success which has attended the efforts of the State Board of Health of Florida in this direction is evidence that the method is practical and of the greatest value to the people. Any physician can easily learn how to make a good blood smear, and if facilities are furnished by the municipality or State for staining and examining them there will be no valid excuse for the neglect of such an examination in any case.

The Treatment of Initial and Latent Infections. A very large proportion of latent infections are the result of untreated or improperly treated initial infections. While, in many instances, the plasmodia may be found in the blood for several days before the onset of an initial infection, it is a fact that most latent infections have been preceded by one or more acute attacks of malaria. The profession is very largely to blame for these cases, in civilized regions, for if the initial attack had been properly treated no plasmodia would have survived, and thus latent infections would have been prevented. As showing the large proportion of such infections in patients who have suffered from malarial paroxysms, I may mention observations[12] made at the United States Army General Hospital in San Francisco, and in the Philippine Islands. Of 1,653 patients showing plasmodia in the blood, 424, or a little over 25 per cent, presented no symptoms of the disease at the time of examination, or, in other words, 25 per cent of the patients presented latent infections. All of these pa-

tients had suffered from acute attacks of malaria, and the only conclusion possible was that most of them had not been properly treated during such attacks, or the disease would not have become latent, for the vast majority were examined in San Francisco where reinfections could be excluded, as malaria is not prevalent there, and several weeks had elapsed since they had left the Philippine Islands. Many of these patients were *gamete* carriers, and were thus able to infect mosquitoes.

It will thus be seen that the proper treatment of initial infections is of immense importance in the prophylaxis of malarial disease. The forms of the plasmodia which are capable of undergoing development in the mosquito, or the *gametes,* do not develop in the blood of man unless the infection has lasted for a period of several days (from 9 to 15), and it is obvious that if we can kill the plasmodia before *gametes* develop our patients will not become carriers of the infection. On the other hand, if they are untreated, or improperly treated, *gametes* will develop sooner or later, in most instances, and the patients will become a constant source of danger to those associated with them.

A very great deal of the malaria prevalent in every locality where civilization exists is directly traceable to improperly treated patients. The practice of regarding malarial infections as cured because the active symptoms have disappeared is a most common and a most pernicious one, and one that is responsible for the transmission of a very large proportion of malarial disease. It is but too true that the medical profession is largely to blame for this error, for nothing is more common than to observe malarial patients walking about after only a day or two of treatment, inquiry eliciting the fact that the attending physician has given no directions whatever concerning the continued use of quinine. It must be remembered that *all* malarial infections are resistant to treatment; that the mere disappearance of the symptoms is no index of the destruction of all the plasmodia which may be present; and that a continued course of quinine is absolutely necessary to rid the system of even the mildest malarial infection.

The proper treatment of *latent* infections is of as great importance as that of initial infections and should follow the same general lines, but in too many of these cases *gametes* have already developed, and these, as is well known, are very resistant to quinine, and therefore it will have to be continued for a longer time, and the outlook, so far as preventing the infection of the mosquito, is less favorable. The researches of Darling show that the continuous administration of quinine in full doses to *gamete* carriers for a considerable time, results in reducing the number of *gametes* to a non-infective minimum, but it is much easier to prevent their development by the proper treatment of the initial infection than it is to destroy them after they have once been developed. However, in all latent infections quinine should be administered as in active infections until the plasmodia have disappeared. It is these cases which are continually infecting the mosquitoes, and thus increasing the number of human infections, and unless these "carriers," as they may be called, are discovered and properly treated, it is almost hopeless to attempt to rid any locality of malaria where mosquitoes cannot be eradicated. The following methods of treatment will be found most efficacious in initial and latent infections.

In tertian and quartan malaria, quinine should be given in doses of 0.32 gm. (gr. V) every four hours until 1 to 2 gm. (gr. XV to XXX) is given within the twenty-four hours, and this amount continued until the active symptoms or the plasmodia have disappeared. After this the drug should be continued in doses of 0.65 gm. (gr. X) every day for two weeks, and in doses of 0.32 gm. (gr. V) every day for two weeks longer. For two or three months thereafter 0.65 gm. (gr. X) of quinine should be taken once a week.

In æstivo-autumnal infections, unless pernicious symptoms be present, quinine should be given by the mouth in doses of 0.32 gm. (gr. V) every four hours until active symptoms or the plasmodia have disappeared. For the next two weeks 1 gm. (gr. XV) of quinine should be taken daily, and for two weeks thereafter 0.65 gm. (gr. X) every night on retiring. For at least two months thereafter the drug should be administered in doses of 0.32 gm. (gr. V) daily.

In those latent cases in which *gametes* are numerous (more than one to 500 leucocytes) it will be necessary to take larger doses of the drug, as Darling found that it required daily doses of 2 gm. (gr. XXX) continued for two or three weeks to reduce their number to a non-infective ratio.

All malarial infections should, if possible, be isolated in a screened room while the blood contains the plasmodia, in order to prevent the infection of mosquitoes. In many instances, especially of latent infection, this precaution cannot be observed, but it should always be insisted upon when conditions are such as to render it practical.

The Education of the Public. I have noted the importance of the discovery of latent malarial infections and their treatment, but unless an enlightened public opinion supports the physician his efforts in this direction will meet with failure.

All of our methods of malarial prophylaxis depend for their success upon the support of the public, and it is the duty of the medical profession to so present this subject that the public will not only desire, but will demand that proper measures be taken for the prevention of these infections. The same methods which have been so useful in educating the public to the importance of the hookworm can be just as advantageously used in the campaign against malaria.

Educational measures should be instituted by the State boards of health, and as a means to this end, the appointment of a commission composed of physicians for the study of the extent of malarial infections in the State and the methods most suitable for combating them, is an essential. Such commissions should be connected with the State boards of health and should ascertain the amount of malaria present in each locality, the most practical methods of prophylaxis, and the expense of instituting such methods. The reports of the commission should be published as public documents and widely circulated among the people.

Addresses upon the prophylaxis of the malarial fevers, illustrated by lantern slides showing the development of the plamodia in both man and the mosquito, as well as the mosquitoes concerned in transmission, should be given by qualified physicians, and will be found one of the most efficient methods of public education that we possess. The members of the State commission could be sent from place to place for this purpose and the expense involved would be amply repaid by the good accomplished.

Bulletins published by municipal and State boards of health, explaining the etiology and methods of prevention of malaria should be sent to every householder, and such bulletins should be well illustrated and contain in small compass the essential rules for malarial prophylaxis.

That such methods of public education are practicable have been proven by the State Board of Health of Florida. In that State a commission was appointed by the State Medical Association for the study of malaria and the State Board of Health has recently published a most excellent bulletin upon these fevers for public distribution, a bulletin which must result in great good to the people of that State.

The economical damage done any community by the prevalence of the malarial fevers should be dwelt upon in addresses and bulletins, and statistics illustrating this point should be collected and distributed among the people. Attention should be called also to the grave

complications which follow repeated malarial infections, resulting in the invalidism of a large proportion of the inhabitants of badly infected districts.

The public press possesses great power in this country, a power which is at the disposal of the medical profession in the campaign against malaria. It has always been the experience of sanitarians that the newspapers are more than willing to assist in any project looking toward the conservation of public health, and welcome contributions which instruct the people in the prevention of disease. I am very sure that the papers of every State in which malaria is prevalent would freely open their columns to contributions regarding prophylaxis and would loyally support all proper efforts for the prevention of these fevers. The help thus afforded in public education would be almost incalculable, while the active support of the press would make possible measures which otherwise would result in failure.

The teaching of the essentials of malarial prophylaxis in the public schools, in regions in which these fevers are endemic, is a most useful method of public education. The young are receptive and there is no better way of interesting the parents than by the instruction of the children. Not only is this true, but what one learns in youth becomes a matter of habit and will be practiced throughout life. The adage that "You cannot teach an old dog new tricks," is often exemplified when attempts are made to instruct the adult population in modern views of the etiology and prophylaxis of disease, and for this reason it is most important that the young be thoroughly taught regarding the prophylaxis of malaria.

Members of the medical profession may accomplish a vast amount of good by missionary work among the people in the localities in which they are practicing. A few words of instruction regarding the etiology of malaria, and directions for applying prophylactic measures in the home, will often do more for the cause than either lectures or bulletins. In this matter the profession has more than a nominal interest, for the presence of much malarial infection in any place is really a reflection upon the ability, public spirit, and activity of the medical practitioners of that locality.

The notification of cases of malaria would do much toward impressing the public with the importance of these infections. Every case of malaria should be reported to the health authorities, and they should be empowered to enforce proper precautions against its transmission, as is done in other infectious diseases. Such notification would focus the attention of the public and lead to the conviction that these fevers are really infectious and a serious menace to the community.

The creation of a national commission for the study of malaria as it occurs in the United States, first suggested, I believe, by your Secretary, Dr. Seale Harris, would prove of inestimable benefit to the entire country. Such a commission could investigate the fevers prevalent in malarial regions with a view to determining the proportion actually due to malarial infection, and the methods of prophylaxis which could be most economically and successfully employed in the endemic centers. A malarial survey of the entire country could thus be secured and an intelligent effort could then be made to eradicate the disease. At the present time the greatest confusion exists regarding the prevalent fevers of many localities in the United States, and if nothing more were accomplished by the commission than a scientific classification of these fevers, a great good would be accomplished, and the appointment of such a commission amply justified.

In Italy the function of a national commission has been fulfilled by a national society known as the Society for the Study of Malaria. This society has the support of the government and controls malarial prophylaxis throughout Italy. Its efforts have been crowned with such success that the mortality of malaria has diminished almost 75 per cent,

from 16,000 deaths annually to about 4,000, while there is probably no one so ignorant in that country as to doubt the efficiency of the methods instituted for the suppression of the disease, or who does not know why they were instituted and how they are proving successful.

I believe that the time is not far distant when we will equal Italy in our application of malarial prophylaxis, and when such regions as the beautiful Mississippi delta, now ravaged by the most pernicious forms of malarial fever, will be as free from these infections as the more northern parts of our country. Malaria is a preventable disease, and the earnest and intelligent application of prophylactic measures *must* result in its ultimate disappearance. Celli has well said that the prophylaxis of malaria is a purely economical question, and that any community which cares to spend the money can rid itself of the disease. Fortunately, as shown by Colonel Gorgas, the cost is not excessive, even in the most badly infected localities, for he estimates that the cost for sanitation on the Isthmus has averaged $3.50 *per capita* annually, of which $2.00 was spent upon mosquito destruction. When one remembers that this expenditure has resulted in the disappearance of yellow fever and a reduction in the death rate of malaria from 16.21 per thousand to less than 2. per thousand, the cost sinks into insignificance.

We now know the etiological factors concerned in the production of the malarial fevers and their method of transmission, and we also know that proper prophylactic methods have been followed by the disappearance of the infection from numerous localities. I believe, therefore, that it is simply a question of time when the malarial fevers will be as rare in civilized countries as are now some of the acute infectious diseases, and that eventually these infections will disappear. Italy has pointed out to the world the proper legislative control of this disease, which rendered her lands barren in the past and destroyed thousands of her inhabitants, and the enforcement of similar prophylactic measures in this country will be followed by equally successful results.

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